Designing Microfluidic Devices for Drug Diffusion Testing

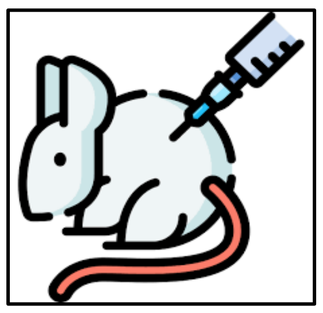
Authors list: Rindhiya Vishnu Shankar (BEng)
Project supervisor: Davide Carta (PhD) & Prof Julien Gautrot

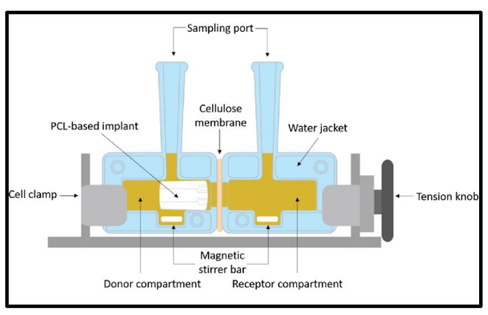
Queen Mary University of London

QMCUR

Introduction

Drug diffusion testing is crucial for predicting the real-world performance, efficacy, and safety of pharmaceutical compounds. Conventional diffusion testing methods such as in vivo animal models and in vitro Franz cells are often time-consuming, expensive, and difficult to reproduce.

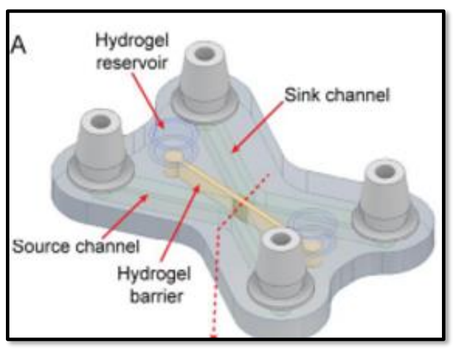


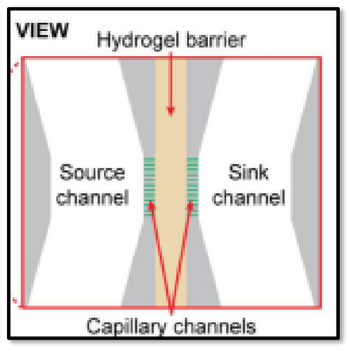


Microfluidic devices offer a promising alternative by miniaturising testing environments to mimic physiological diffusion processes using small sample volumes. This project focuses on developing a microfluidic chip that enables efficient, reproducible, and scalable drug diffusion testing using hydrogel-based barriers that replicate biological tissue characteristics

Literature Review

Existing microfluidic diffusion models commonly feature three-channel designs comprising source, sink, and central hydrogel regions.





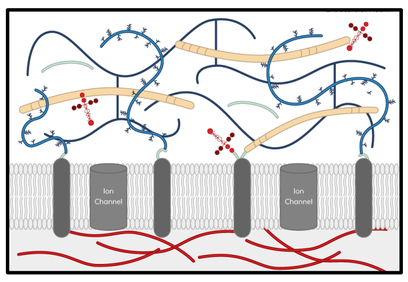
- **Source**: Where drug is placed
- **Sink**: Where the diffused drug is collected
- **Central**: Custom Hydrogel Barrier that acts as a selective filter.

The hydrogel barrier, typically made from PEG-DA or agarose, allows selective diffusion of molecules while maintaining separation of fluids through surface tension effects. Hydrogels barriers are valued for their easily tuneable porosity, optical transparency and ability to mimic extracellular matrices.

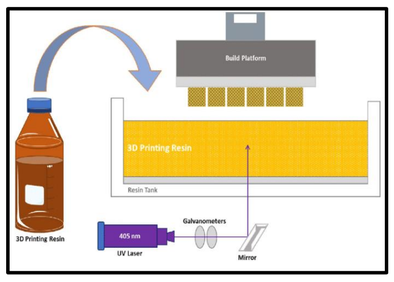
Why Hydrogel Barrier, Why NOT culture living cells instead ?

1. Complicates Reproducibility
2. High Resource and Time Requirement
3. Relatively Expensive

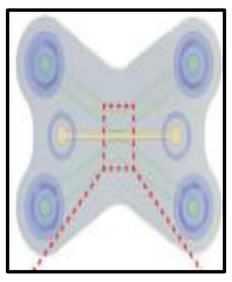
Design Objectives



Use hydrogels that mimic the extracellular matrix better



For large scalability, produce chips using off the shelve resin



Easy for lab technicians to apply resin and seal the 3D-printed chip to the Aptes-coated glass slide

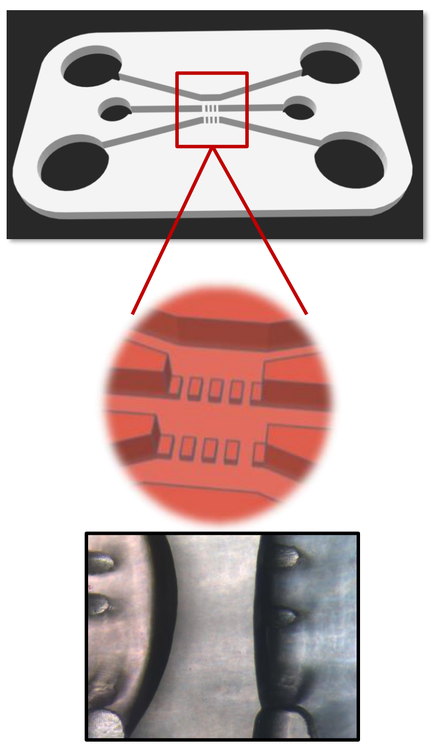
Methodology

The experimental process began with computer-aided design (CAD) of the microfluidic chip in Fusion 360, followed by fabrication using a **DLP 3D printer** with an **off-the-shelf clear resin** (MULTICOMP MP004390). After printing, the device was UV post-cured and bonded to an APTES-coated glass slide to create a sealed microchannel system. The central channel was filled with a **fibrin-based hydrogel** formed by mixing fibrinogen and thrombin, while phosphate-buffered saline (PBS) solutions with coloured dyes were introduced into the source and sink channels to visualize diffusion.

Prototype Testing

Design Iteration 1

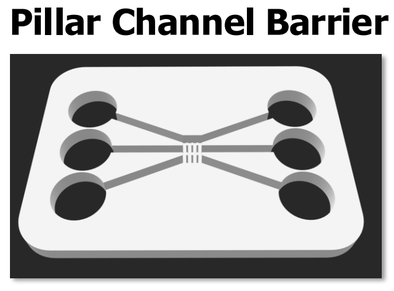
Pillar Channel Barrier **Phase Guide Barrier**

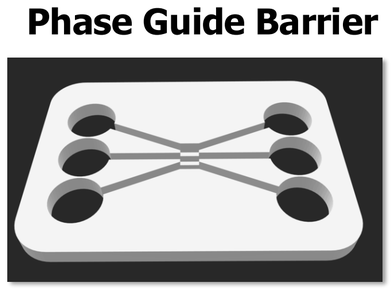


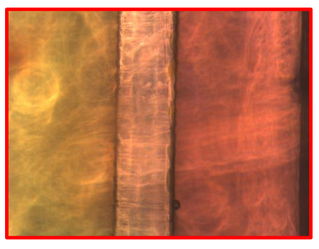
Limitation: Fibrin Gels before reaching centre because inlets are too small

Design Iteration 2

Pillar Channel Barrier **Phase Guide Barrier**



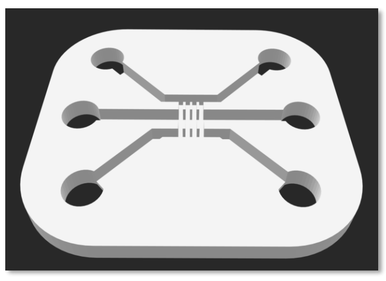


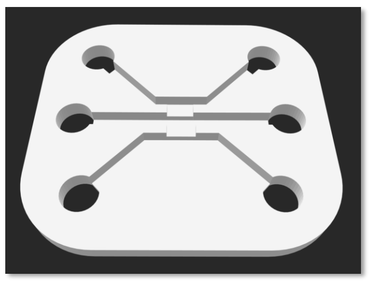


Limitation: Difficult to apply resin and seal the chip to Aptes-glass slide.

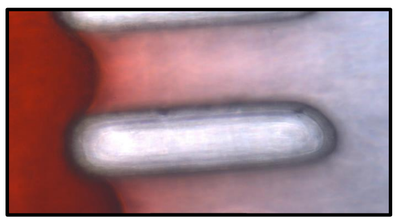
Design Iteration 3

Pillar Channel Barrier **Phase Guide Barrier**





Results with fibrin hydrogel:



Observation: Inward meniscus formed.

Results with organo-hydrogel:

Observation: Meniscus formed faster; diffusion happened slower.

Limitation: Difficult to apply resin and seal the chip to Aptes-glass slide.

Future Work

1. Develop a more curved design to apply resin easier
2. Height of Inlets/Outlets should increase to accommodate more hydrogel.

Reference

[1] Kim, Y.T., Bohjanen, S., Bhattacharjee, N. and Folch, A. (2019). Partitioning of hydrogels in 3D-printed microchannels. *Lab on a Chip*, 19(18), pp.3086–3093. doi:https://doi.org/10.1039/c9lc00535h.

[2] Kalossaka, L.M., Mohammed, A.A., Sena, G., Barter, L. and Myant, C. (2021). 3D printing nanocomposite hydrogels with lattice vascular networks using stereolithography. *Journal of Materials Research*, 36(21), pp.4249–4261. doi:https://doi.org/10.1557/s43578-021-00411-2.